U.S. Illnesses and Deaths Associated With Compounded or Repackaged Medications, 2001-17

Update note: This chart was updated in March 2018 to include newly reported adverse events, and newly reported details of previously included adverse events. The updated chart also replaced the term "pharmacy" with "compounder," to reflect the fact that drugs can be compounded by physicians and outsourcing facilities in addition to pharmacies.

Pew's drug safety project has identified more than 71 reported compounding errors or potential errors associated with 1,416 adverse events, including 115 deaths, from 2001 to 2017. However, a 2015 survey found that only 30 percent of states (13 of the 43 that responded) require sterile compounding pharmacies to report serious adverse events.[1] Of the states that require reporting, the type of information that is required to be reported may vary, further contributing to an incomplete picture of adverse events associated with compounded medications. Even in states with strong adverse event reporting requirements, illnesses and deaths caused by compounded drugs are not always linked to the compounding error.[2,3,4] Because many such events may go unreported, this chart is likely an underestimation of the number of compounding errors since 2001. Contamination of sterile products was the most common error; others were the result of pharmacists' and technicians' miscalculations and mistakes in filling prescriptions.

Drug compounding can be an interstate operation; pharmacies may prepare medicines in one state and ship them to another. States may encounter oversight challenges if an out-of-state pharmacy shipping into their jurisdiction is held to a different quality or regulatory standard than in-state compounders. As a result, for each row below, the state where the compounding error or potential error occurred and the state(s) where the adverse event(s) occurred are listed. Harmonized minimum quality standards for anyone who compounds drugs in any setting across states would help address challenges in regulating out-of-state pharmacies and ensure that all compounding meets strong baseline criteria for preparing safe drugs and protecting patients.

Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2017	2		Tissue erosion at injection site	High pH; no glutamine detected in samples[5]	Compounded injectable of glutamine, arginine, and carnitine (GAC)	FL	Not reported	
2017	1[6]		Hemorrhagic occlusive retinal vasculitis (HORV)	Not reported	Intraocular injectable of triamcinolone, moxifloxacin, and vancomycin (TMV)	NJ	Not reported	

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2017	41		Septic arthritis	Bacterial contamination[7]	Unknown injectable	NJ	NJ	Investigation revealed inappropriate use and handling of pharmacy bulk packaged products.
2017	1		Paralysis (partial: face)	Not reported[8]	Compounded injectable	TX	TX	
2017	2	1	One case of cardiac arrest; both experienced immediate hypersensitivity reactions	Product contained ungraded PEG 40 castor oil[9]	Injectable curcumin emulsion infusion	CA	Not reported	
2017	At least 43[10]		Vision impairment, poor night vision, loss of color perception, photophobia, ocular discomfort, nausea, loss of balance, and other symptoms	Unknown[11]	Injectable steroid antibiotic for administration in the eye	TX	TX	
2016	6[12]	1	Septic arthritis	Contamination	Viscosupplementation knee injectable	Not reported	SC	
2016	1		Abscesses and osteomyelitis	Contamination[13]	Unknown injectable		NM	Investigation revealed unsafe injection and compounding practices.
2016	7		Thyrotoxicosis[14]	Super-potent compounded drug	Compounded oral liothyronine	SD	Not reported	

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2016	17	2[15]	Fungal bloodstream infections	Contamination[16]	Injectable saline, heparin, vancomycin, and ceftazidime	NY	NY	IV flush solutions were not compounded under quality standards set by the United States Pharmacopeial Convention and were used past appropriate beyond-use dating. The two deaths occurred within 12 weeks of the fungal infection, but it is unclear whether the deaths were a result of the infections.
2016[17]	1		Overdose	Dose of manganese chloride 1,000 times stronger than usual dose[18]	Injectable manganese chloride	Not reported	Not reported	High manganese dose of 800 mg, compared with usual dose of 0.15-0.8 mg/day. Patient showed no resulting symptoms, but manganese overdose can result in side effects on the nerves and brain.
2016	3		Unspecified serious adverse events	Dose of morphine sulfate stronger than labeled concentration[19]	Injectable morphine sulfate	IN	IL, IN[20]	
2015	5		Redness, swelling, and pain at injection site[21]	Contamination	Compounded betamethasone phosphate and betamethasone acetate	AL	Not reported	
2015	"Several"[22]		Unspecified	High dose of vitamin D_3[23]	Oral multivitamin capsule	FL	Nationwide[24]	High vitamin D_3 can cause significant short- and long-term effects.
2014-15	7		Hepatitis C	Contamination[25]	Unknown injectable	CA	CA	Investigation into the clinic revealed infection control breaches and ongoing issues with infection control practices.
2014-15	"Several"[26]		Unspecified	Contamination[27]	Sterile products	AL	Nationwide[28]	Administration of contaminated sterile products may result in serious and potentially life-threatening infections or death.

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2014	"Several"[29]		Toxicity	Adulterated and misbranded drug (contained different API)	L-Citrulline	NY	Not reported	Samples of the product were found to contain a different amino acid (N-Acetyl-Leucine) than what the label claimed.
2014	1	1	Toxicity[30]	Not reported	Compounded topical anesthetic cream (ketamine)	TX	TX	
2014	At least 37[31]		Not reported	Contamination	Intravitreal injections of bevacizumab or ranibizumab	FL	Not reported	Bevacizumab and ranibizumab were repackaged in a manner that exposed sterile, preservative free vials to an uncontrolled environment.
2014	1		Severe flushing, stinging, and dizziness[32]	Dose of magnesium sulfate 200 percent stronger than labeled concentration[33]	Compounded magnesium sulfate injectable	TX	Not reported	
2014	Unknown		Oversedation	Dose of midazolam labeled with incorrect concentration[34]	Injectable midazolam	IN	Not reported	Compounded midazolam, a sedating agent, did not match the concentration on the product label. Oversedation can result in a range of effects from increased sleepiness to severe difficulty breathing.
2013	1		Bacterial bloodstream infection	Contamination[35]	Injectable mineral product	TX	CA	Voluntary recall of injectable mineral product that contained bacteria with the potential for serious infection. A patient was admitted to the hospital with an infection of the same bacteria.
2013	15	2[36]	Bacterial bloodstream infection	Contamination[37, 38,39]	Injectable calcium gluconate	TX	TX	The Centers for Disease Control and Prevention has not conclusively linked the deaths to the contaminated drug.

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2013	6		Fever, flu-like symptoms, soreness at injection site	Unknown[40,41]	Injectable methylcobalamin	TX	Not reported	A compounded injection was recalled due to complaints of fever, flu-like symptoms, and soreness at the injection site. Subsequent Food and Drug Administration inspection found that sterility and quality of the manufacturing process could not be assured.
2013	5		Serious bacterial eye infections	Contamination[42, 43,44]	Injectable bevacizumab for administration in the eye	GA	IN	
2013[45]	8		Fungal eye infections	Contamination[46]	Injectable bevacizumab-triamcinolone for administration in the eye	Not reported	NY	Fungal infection of the eye caused significant visual impairment that persisted for at least three months from the incident.
2013[47]	1		Kidney failure and acute injury of the liver and pancreas	Unknown[48]	Injectable combination product for administration under the skin	Not reported	Not reported	Product is marketed for dissolving fat. The patient developed difficulties with digestion and metabolism as well as kidney failure, which required dialysis.
2012-13	12		Bacterial bloodstream infection	Contamination[49]	Parenteral infusion	Not reported	IL	Facility inspection revealed deficiencies in the parenteral medication preparation and handling.
2012-13	778[50]	76	Fungal meningitis and other infections	Contamination[51,52]	Injectable preservative-free methylprednisolone acetate	MA	FL, GA, ID, IL, IN, MD, MI, MN, NC, NH, NJ, NY, OH, PA, RI, SC, TN, TX, VA, WV	Additional products (betamethasone, cardioplegia, and triamcinolone solutions) produced at the facility were also found to be contaminated, but adverse events linked to these products have not been reported.[53]
2012-13	26		Bacterial and fungal infections in skin and soft tissue	Contamination[54]	Injectable preservative-free methylprednisolone acetate	TN	AR, FL, IL, NC	Skin and soft tissue infections resulted after intramuscular injection of preservative-free product. Subsequent voluntary recall of sterile products was issued.

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2012	47		Fungal eye infection; vision loss in majority of cases	Contamination[55]	Injectable brilliant blue-G (BBG) retinal dye and triamcinolone for administration in the eye	FL	CA, CO, IL, IN, LA, NC, NV, NY, TX	
2012	7		Bacterial bloodstream infection	Contamination[56]	Injectable fentanyl	NC	NC	
2012[57]	1		Overdose	Dose of flecainide four times stronger than ordered[58]	Oral flecainide liquid	Not reported	Not reported	Flecainide toxicity can cause abnormal heart rate and rhythms that can be severe and life-threatening, as well as increased liver enzymes, which can be an indicator of liver injury.
2012	10	1	Bacterial bloodstream infection	Contamination[59]	Contrast dye, anesthetic and steroid injections, single-dose vials	Not reported	AZ, DE	The outpatient pain clinic failed to follow Standard Precautions[60] by using single-dose vials as multi-dose vials.
2011-12	15		Bacterial bloodstream infection	Contamination[61]	Saline flush	Not reported	WV	Adverse events resulted from the use of bulk saline bag for IV flushes in a physician office practice.
2011[62]	1		Toxicity	Dose of 4-aminopyridine 10 times stronger than labeled concentration[63]	Oral 4-aminopyridine pills	Not reported	Not reported	Patient experienced stomach pain, anxiety, extreme sweating, and slow heart rate prior to developing life-threatening seizures. Following a complicated hospital stay, the patient sustained permanent short-term memory loss.
2011[64]	9		Bacterial eye infection, and one case of meningitis and encephalitis; four cases of loss of eyesight	Contamination[65]	Injectable bevacizumab for administration in the eye	Not reported	TN	

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2011	12		Bacterial eye infection; three patients had eye removals	Contamination[66]	Injectable bevacizumab for administration in the eye	FL	FL	
2011	5		Blindness	Unintended presence of another medication[67]	Injectable bevacizumab for administration in the eye	CA	CA	Trace amounts of bortezomib, a cancer drug that is not intended for injection into the eye, were detected on a sample syringe.
2011	19	9	Bacterial bloodstream infection	Contamination[68]	Parenteral nutrition solution	Not reported	AL	
2010	1	1	Fatal overdose	Dose of sodium 60 times stronger than ordered[69]	Injectable sodium chloride	IL	IL	Acute sodium overload can cause symptoms ranging from fluid retention to seizures and coma, affecting multiple organs including lungs and kidneys. The patient was exposed to a potent sodium-containing fluid that was entered incorrectly during the preparation of the medication, resulting in death.
2010	1		Unspecified side effects	Dose of liothyronine 10 times stronger than ordered[70]	Oral liothyronine (T3)	AZ	AZ	Liothyronine overdose can result in shakiness, increased heart rate, and palpitations.
2009	1	1	Fatality	Unknown[71]	Injectable hydromorphone	TN	Not reported	
2009	1	1	Fatal overdose	Dose of levothyroxine 18 times stronger than ordered[72]	Oral levothyroxine pills	NC	NC	
2009	9		Eye infection; at least one case of vision loss	Unknown[73]	Injectable preservative-free hyaluronidase for administration in the eye	FL	Not reported	Patients developed orbital cellulitis, a type of infection that results in inflammation of the eye.
2008[74]	1		Acute withdrawal	Dose of baclofen 7 percent of ordered dosage[75]	Injectable baclofen for administration in the spine	Not reported	Not reported	The product included a fraction of the intended dose of baclofen. Patient experienced frequent and severe spasms.

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2008	1	1	Fatal overdose	Dose of sodium chloride 10 times stronger than ordered[76]	Injectable sodium chloride	NC	NC	Acute sodium overload can cause symptoms ranging from fluid retention to seizures and coma, and affect multiple organs including lungs and kidneys.
2008[77]	1		Persistent inflammatory reaction	Unknown[78]	Mesotherapy injections	Not reported	CO	Seven months after receiving mesotherapy injections, patient developed a persistent immune-mediated inflammatory reaction.
2007[79]	1	1	Fatal acute respiratory distress syndrome	Colistimethate sodium left in solution longer than recommended[80]	Colistimethate sodium inhaled solution	Not reported	Not reported	The prodrug of colistin is better tolerated than the active drug to which it converts. More than half of the prodrug is converted within two days in solution at a certain temperature. This premixed product was in solution for five weeks before further dilution for administration.
2007	3	3	Fatal overdose	Dose of colchicine eight times stronger than labeled concentration[81]	Injectable colchicine	TX	OR, WA	IV doses that exceed the standard single-use therapeutic dose of 2-4 mg per episode of gout have resulted in life-threatening toxicity. In this case, the doses were eightfold these limits.
2007	8	1	Bacterial bloodstream infection	Contamination[82]	Injectable fentanyl	Not reported	CA, MD	
2006	1		Decreased consciousness, low blood pressure, and lack of oxygen	Mislabeled product leading to administration of different drug than ordered[83]	Epidural morphine sulfate (fentanyl/bupivacaine was ordered)	MS	AZ	Both fentanyl and morphine are in the same class of sedative analgesics. The symptoms of decreased consciousness, hypoxia, and hypotension are consistent with higher than intended opioid exposure.

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2006	At least 70		Redness, swelling, bruising, rash, fever, and cellulitis	Betamethasone made with incorrect amount of preservative[84,85]	Injectable betamethasone	AL	Not reported	The product was voluntarily recalled, and a subsequent reformulation continued to include an incorrect amount of preservative. An FDA investigation discovered at least 70 complaints associated with the drug.
2006	1	1	Fatal overdose	Dose of chemotherapy infusion diluted with toxic amount of sodium chloride[86]	Chemotherapy infusion	OH	OH	Acute sodium overload can cause symptoms ranging from fluid retention to seizures and coma, and affect multiple organs including lungs and kidneys.
2006	1	1	Fatal overdose	Dose of zinc 1,000 times stronger than ordered[87]	Neonatal parenteral nutrition solution	NV	NV	The dose was incorrectly entered for pharmacy preparation as milligrams instead of micrograms, resulting in a thousandfold overdose.
2005	3	1	Fatal overdose, cardiac arrest	Dose of lidocaine and tetracaine higher than usual[88,89]	Topical combination anesthetic creams (lidocaine and tetracaine)	NC	NC	
2005	19	1	Bacterial bloodstream infection	Contamination[90,91]	Injectable magnesium sulfate	TX	CA, MA, NC, NJ, NY, SD	
2004-06	80		Bacterial bloodstream infection	Contamination[92]	Injectable heparinized saline	TX	MI, MO, NY, SD, TX, WY	

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2004-05	6		Bacterial eye infection; all cases had partial or complete loss of vision; two patients had eye removals	Contamination[93]	Trypan blue eye drops	Not reported	Not reported	
2004-05	11	3	Systemic inflammatory response syndrome	Contamination[94,95]	Cardioplegia solution for administration during heart surgery	MD	VA	
2004	2		Bacterial bloodstream infection	Contamination[96]	Injectable heparin-vancomycin	FL	CT	
2003	2		Overdose	Dose of liothyronine stronger than ordered[97]	Oral liothyronine (T3) pills	AZ	AZ	Unused pills of both patients were analyzed, and the concentration of the active ingredient was found to be 800 and 900 times higher than intended. High T3 levels can result in shakiness, increased heart rate, and palpitations.
2002-04	1	1	Fatal overdose	Dose of lidocaine and tetracaine higher than usual[98,99]	Topical combination anesthetic cream (lidocaine and tetracaine)	UT	AZ	
2002[100]	1		Toxicity	Dose of clonidine 10 times higher than ordered[101]	Oral clonidine capsules	Not reported	Not reported	Patient showed early signs of central nervous system depression (such as drowsiness) and miosis (constricted or small pupils).

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2002[102]	1		Toxicity	Dose of clonidine 87 times higher than ordered[103]	Oral clonidine liquid	Not reported	Not reported	Patient showed signs of central nervous system depression, consistent with severe clonidine toxicity. Miosis (constricted or small pupils) was also noted.
2002	2		Meningitis	Contamination[104]	Injectable methylprednisolone for administration in the spine	MI	MI	
2002	7	2	Fungal meningitis and sacroiliitis	Contamination[105,106,107]	Injectable methylprednisolone acetate for administration in the spine	SC	NC	
2001	2		Bacterial bloodstream infection	Contamination[108]	Injectable preservative-free heparinized saline	Not reported	Not reported	
2001[109]	1		Overdose	Dose of clonidine 1,000 times stronger than ordered[110]	Oral clonidine liquid	Not reported	Not reported	During preparation of liquid clonidine from solid pills, milligrams were substituted for micrograms, resulting in a thousandfold overdose. Patient's initial presentation included hyperventilation, an unusual feature of clonidine toxicity. Severe clonidine toxicity can result in low blood pressure, central nervous system depression (lethargy, mental status changes), and cardiopulmonary instability (heart and breathing problems).

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Year	Reported cases	Reported deaths	Adverse events	Compounding error	Product	State where compounding occurred	State where adverse event(s) occurred	Notes
2001	13	3	Five cases of meningitis; five cases of epidural abscess; one patient had an infected hip joint; two unspecified	Contamination[111,112]	Injectable betamethasone for administration in spine or joint	CA	CA	
2001	4		Bacterial bloodstream infection	Contamination[113]	Injectable ranitidine	Not reported	Not reported	
Total	**1,416**	**115**						

This chart includes U.S. illnesses and deaths associated with compounded or repackaged medications from 2001 to 2017. Adverse events were drawn from FDA and CDC resources as well as journal and news articles.

In the total, "several" reported cases were counted as two adverse events, and an "unknown" number of reported cases were counted as zero adverse events.

Endnotes

1. The Pew Charitable Trusts, "National Assessment of State Oversight of Sterile Drug Compounding" (2016), http://www.pewtrusts.org/~/media/assets/2016/02/national_assessment_of_state_oversight_of_sterile_drug_compounding.pdf.
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5. U.S. Food and Drug Administration, "FDA Investigates Two Adverse Events Associated With United Pharmacy's Compounded Glutamine, Arginine, and Carnitine Product for Injection," accessed Nov. 14, 2017, https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm584125.htm.
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14. Janet Woodcock and Julie Dohm, "Toward Better-Quality Compounded Drugs — An Update from the FDA," *The New England Journal of Medicine* 377, no. 26 (2017): 2509-2512, http://dx.doi.org/10.1056/NEJMp1712905.

15. The source explicitly states that it is unclear whether the reported deaths were related to the compounding error or potential error.

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20. The drug product was distributed to Illinois and Indiana; information was not available about where adverse events occurred.

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22. The source explicitly states that the adverse events were potentially associated with the compounded drug product in question.

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24. The drug product was distributed nationally; information was not available about where adverse events occurred.

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